

IN THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

Claim 1 (Currently Amended): A process for preparing crystalline desloratadine Form I substantially free of Form II comprising the steps of:

- a) preparing a solution of desloratadine in a solvent selected from the group consisting of acetonitrile, di-methyl formamide, tetrahydrofuran and diethylcarbonate, wherein crystalline desloratadine Form I crystallizes out of the solution; and
- b) recovering the crystalline desloratadine Form I.

Claim 2 (Original): The process of claim 1, wherein the solvent is acetonitrile.

Claim 3 (Original): The process of claim 1, wherein the solvent is di-methyl formamide.

Claim 4 (Original): The process of claim 1, wherein the solvent is tetrahydrofuran.

Claim 5 (Original): The process of claim 1, wherein the solvent is diethylcarbonate.

Claim 6 (Original): The process of claim 1, further comprising a drying step.

Claim 7 (Original): The process of claim 1, wherein the solution is cooled to about 20°C to about 30°C.

Claim 8 (Cancelled).

Claim 9 (Currently Amended): The process of claim 1, claim 8, wherein the ratio of Form II to Form I is less than about 0.5% [[1%]] by weight.

Claim 10 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine, ranges from about 15% to about 25%, said process comprising the steps of:

- a) preparing a solution of desloratadine in ~~a solvent selected from the group consisting of chloroform and ethyl acetate;~~
- b) combining the solution with an anti-solvent to precipitate the crystalline desloratadine; Form I; and
- c) recovering the crystalline desloratadine. desloratadine Form I.

Claim 11 (Original): The process of claim 10, wherein the anti-solvent is a C₂ to a C₈ ether.

Claim 12 (Original): The process of claim 11, wherein the ether is di-isopropyl ether.

Claims 13-14 (Cancelled).

Claim 15 (Original): The process of claim 10, wherein the anti-solvent is a C₅ to a C₁₂ saturated hydrocarbon.

Claim 16 (Original): The process of claim 15, wherein the hydrocarbon is hexane.

Claims 17-23 (Cancelled).

Claim 24 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine, ranges from about 2% to about 10%, said process comprising the step of:

- a) preparing a solution of desloratadine in a C₁ to C₄ alcohol;
- b) combining the solution with water to precipitate the crystalline desloratadine; Form I; and
- c) recovering crystalline desloratadine. Form I.

Claim 25 (Currently Amended): The process of claim 24, wherein the alcohol is ethanol.

Claim 26 (Currently Amended): The process of claim 24, wherein the Form I obtained has from about 2% to about 4% [[10%]] Form II.

Claim 27 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine ranges from about 5% to about 6%, said process comprising the steps of:

- a) preparing a solution of desloratadine in isopropanol,
- b) seeding the solution with Form II to increase the ratio of Form II to Form I; wherein desloratadine Form I the mixture of crystalline desloratadine precipitates from the solution; and

[[b]]

- c) recovering the crystalline desloratadine. Form I.

Claim 28 (Cancelled).

Claim 29 (Original): A process for preparing crystalline desloratadine Form II comprising the steps of:

- a) melting desloratadine to obtain a molten material;
- b) cooling the molten material to obtain a solid; and
- c) grinding the solid.

Claim 30 (Original): A process for preparing a mixture of crystalline desloratadine Form I and Form II comprising the step of grinding crystalline desloratadine Form I.

Claim 31 (Currently Amended): A process for preparing crystalline desloratadine Form II comprising the steps of:

- a) preparing a solution of desloratadine in dimethyl carbonate, wherein desloratadine Form II precipitates from the solution; and
- b) recovering the crystalline desloratadine Form II.

Claim 32 (Currently Amended): The process of claim 31, wherein the crystalline desloratadine Form II recovered is substantially free of Form I.

Claim 33 (Currently Amended): A process for preparing a mixture of crystalline desloratadine composition comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine, ranges from about 15% to about 25%, said process comprising the steps of:

- a) preparing a solution of desloratadine in i-butyl acetate, wherein Form I precipitates from the solution; and
- b) recovering the precipitate.

Claim 34 (Cancelled).

Claim 35 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on

the total amount of desloratadine, ranges from about 2% to about 6%, said process
comprising the steps of:

- a) preparing a solution of desloratadine in a solvent selected from the group consisting of isopropanol and i-butanol, wherein desloratadine Form I precipitates from the solution; and
- b) recovering the crystalline desloratadine. mixture.

Claim 36 (Original): The process of claim 35, wherein the solvent is isopropanol.

Claim 37 (Currently Amended): The process of claim 36, wherein the mixture contains ~~less than~~ about 2% [[10%]] Form II compared to Form I by weight.

Claim 38 (Original): A process for preparing a mixture of crystalline Form I and Form II of desloratadine comprising the step of

drying desloratadine Form I crystals obtained by crystallization from a C₁ to a C₄ alcohol.

Claim 39 (Original); The process of claim 38, wherein the alcohol is isopropanol.

Claim 40 (Original): The process of claim 38, wherein the alcohol is isobutanol.

Claim 41 (Original): A process for making a mixture of crystalline desloratadine Form I and Form II comprising the steps of

combining a solution of desloratadine in a suitable solvent with an anti-solvent containing seeds of both Form I and Form II of desloratadine to precipitate the mixture, and

recovering the mixture.

Claim 42 (Original): The process of claim 41, wherein the mixture contains from about 35% to about 65% Form I by weight.

Claim 43 (Original): The process of claim 41, wherein the solvent is iso-butyl acetate.

Claim 44 (Original): The process of claim 41, wherein the antisolvent is a C₅ to C₁₂ hydrocarbon.

Claim 45 (Original): The process of claim 44, wherein the hydrocarbon is heptane.

Claim 46 (Currently Amended): A process for preparing a mixture of desloratadine crystalline comprising Forms I and II containing at least about 25% of both Form I and Form II, said process of the Forms comprising the steps of:

- a) preparing a solution of desloratadine in a solvent selected from the group consisting of ethyl acetate and iso-butyl acetate, in a mixture with about 3% to about 20% C₁ to C₄ alcohol by volume, wherein the mixture of Form I and II precipitates from the solution; and
- b) recovering the mixture.

Claim 47 (Original): The process of claim 46, wherein the mixture contains at least about 40% of both forms by weight.

Claim 48 (Original): The process of claim 46, wherein the alcohol is present in about 10% by volume.

Claim 49 (Original): The process of claim 46, wherein the alcohol is selected from the group consisting of methanol, iso-propyl alcohol and mixtures thereof.

Claim 50 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) preparing a solution of desloratadine in iso-butyl acetate;
- b) combining the solution with a $[[C_5]]$ C_6 to C_{12} aromatic hydrocarbon to precipitate the mixture, wherein the combining may be carried out before, after or during crystallization; and
- c) recovering the mixture.

Claim 51 (Original): The process of claim 50, wherein the hydrocarbon is heptane.

Claim 52 (Original): The process of claim 50, wherein the mixture contains from about 60% to about 70% Form I by weight.

Claim 53 (Original): The process of claim 50, further comprising increasing ratio of Form II to Form I by seeding the solution with a mixture of Form I and Form II before crystallization.

Claim 54 (Original): The process of claim 53, wherein the seeding results in about 35% to about 45% Form I compared to Form II by weight.

Claim 55 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) preparing a solution of desloratadine in iso-butyl acetate;
- b) combining the solution with iso-butyl acetate at a temperature lower than the solution to crystallize the mixture; and
- c) recovering the mixture.

Claim 56 (Original): The process of claim 55, further comprising seeding the solution with a mixture of Form I and Form II before crystallization.

Claim 57 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) preparing a solution of desloratadine in ethyl acetate;
- b) seeding the solution with a mixture of Form I and Form II;
- c) combining the solution with a C₅ to C₁₂ saturated hydrocarbon,
wherein the combining may be carried out before, after or during crystallization;
and
- d) recovering the mixture of desloratadine Form I and II.

Claim 58 (Original): The process of claim 57, wherein the hydrocarbon is heptane.

Claim 59 (Original): The process of claim 57, wherein the mixture is about a 4:1 to about a 1:3 mixture of Form I to Form II wt/wt.

Claim 60 (Currently Amended): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) preparing a solution of desloratadine in 2-propanol and toluene, wherein the mixture of Forms I and II precipitates from the solution; and
- b) recovering the mixture.

Claim 61 (Original): The process of claim 60, wherein precipitation occurs as a result of cooling the solution.

Claim 62 (Original): The process of claim 60, wherein ratio of 2-propanol to toluene is less than about 20% by volume.

Claim 63 (Original): The process of claim 60, wherein precipitation occurs as a result of adding a C₅ to C₁₂ saturated hydrocarbon as an anti-solvent.

Claim 64 (Original): The process of claim 63, wherein the anti-solvent is n-heptane or n-hexane.

Claim 65 (Original): The process of claim 63, further comprising the step of seeding the solution.

Claim 66 (Currently Amended): A process for preparing a mixture of desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) providing a first solution of desloratadine in toluene;
- b) evaporating the toluene to obtain a residue;
- c) dissolving the residue in a mixture of toluene and a C₁ to C₄ alcohol to obtain a second solution;
- d) cooling the second solution to obtain a slurry; e) combining the slurry with a C₅ to C₁₂ saturated hydrocarbon to precipitate the mixture; and
- f) recovering the mixture.

Claim 67 (Original): The process of claim 66, wherein the alcohol is 2-propanol.

Claim 68 (Currently Amended): A process for preparing a mixture of desloratadine comprising Form I and Form II, said process comprising the steps of:

- a) combining desloratadine acetate, toluene and KOH to obtain a reaction mixture;
- b) heating the mixture, whereby two phases are obtained;
- c) separating the phases;
- d) concentrating the separated organic phase;
- e) dissolving the obtained concentrate in a toluene-2-propanol mixture containing less than about 20% 2-propanol by volume;
- f) cooling the solution to obtain a slurry;
- g) combining the slurry with cold n-heptane; and
- h) recovering mixture of desloratadine forms I and II.

Claim 69 (Original): The stable mixture of claim 68, wherein the process further comprises washing the product of step c with water.

Claim 70 (Original): The stable mixture of claim 68, wherein the process further comprises warming the product of step f to 45°C.

Claim 71 (Original): The process of claim 68, wherein the mixture is about a 24 to about a 40% Form II compared to Form I.

Claim 72 (Original): A process for preparing crystalline desloratadine Form II comprising the steps of crystallizing desloratadine from toluene, and recovering the crystalline form.

Claim 73 (New): The process of claim 29, wherein the crystalline desloratadine Form II is substantially free of Form I.

Claim 74 (New): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine, ranges from about 35% to about 40%, said process comprising the steps of:

- a) preparing a solution of desloratadine in chloroform;
- b) combining the solution with an anti-solvent to precipitate the mixture of crystalline desloratadine; and
- c) recovering the mixture of crystalline desloratadine.

Claim 75 (New): The process of claim 74, wherein the anti-solvent is a C₂ to a C₈ ether.

Claim 76 (New): The process of claim 75, wherein the ether is di-isopropyl ether.

Claim 77 (New): The process of claim 74, wherein the anti-solvent is a C₅ to a C₁₂ saturated hydrocarbon.

Claim 78 (New): The process of claim 77, wherein the hydrocarbon is hexane.

Claim 79 (New): The process of claim 74, wherein the solution has an initial temperature of at least about 40°C.

Claim 80 (New): A process for preparing a mixture of crystalline desloratadine comprising Form I and Form II, wherein the amount of Form II, based on the total amount of desloratadine, ranges from about 2% to about 6%, said process comprising the steps of:

- a) preparing a solution of desloratadine in chloroform;
- b) combining the solution with an anti-solvent to precipitate the mixture of crystalline desloratadine; and
- c) recovering the mixture of crystalline desloratadine.

Claim 81 (New): The process of claim 80, wherein the anti-solvent is a C₂ to a C₈ ether.

Claim 82 (New): The process of claim 81, wherein the ether is di-isopropyl ether.

Claim 83 (New): The process of claim 80, wherein the anti-solvent is a C₅ to a C₁₂ saturated hydrocarbon.

Claim 84 (New) The process of claim 83, wherein the hydrocarbon is hexane.

Claim 85 (New) The process of claim 80, wherein the solution has an initial temperature of less than about 40°C.

Claim 86 (New) The process of claim 80, wherein the amount of Form II is about 2% wt/wt.

Claim 87 (New) The process of claim 80, wherein the amount of Form II is about 2% wt/wt.

DISCUSSION OF THE AMENDMENT

The Specification is amended in order to correct a typographical error so that the expression "C₅ to C₁₂ aromatic hydrocarbon" found at page 6, lines 3-7; page 8, lines 1-4; and page 19, lines 17-23 reads as "C₆ to C₁₂ aromatic hydrocarbon." Support for the amendment is found at page 8, line 3, in which "benzene" a C₆ hydrocarbon is recited.

Claims 1-72 are pending. Upon entry of the amendment, claims 1-7, 9-12, 15-16, 24-27, 29-33, 35-87 will be pending due to cancellation of claims 8, 13-14, 17-23, 28, and 34, as well as addition of new claims 73-87.

Support for new claims 74-87 is found in original claims 10 and 17-23 and page 9, lines 24ff.

Support for other amendments are as follows: claim 1 to include "substantially free of Form II" is found in original claim 8 (the Examiner's attention is directed to page 11, lines 18-21 for the definition of "substantially free"); claim 9 to change "1%" to read "0.5%" is found at page 11, lines 20-21; claim 10 for the expression "ranges from about 15% to about 25%" is found at page 9. lines 24-26; claim 26 to change "10%" to read "4%" is found at page 9, line 31; claim 27 to include the range "about 5% to about 6%" is found at page 10, line 17, while "step b) is supported in original claim 28; claim 33 to include the range "about 15% to about 25%" is found at page 10, line 5; claim 35 to include the range "about 2% to about 6%" is found at page 10, lines 16-19; claim 37 to change "10%" to read "2%" is found at page 10, line 18; claim 46 to include the expression "Form I and Form II" is found at page 5, lines 29-31; claim 50 changing "C₅ to C₁₂" to read "C₆ to C₁₂" is found at page 6, lines 3-7.

No new matter is believed to be added upon entry of the amendment.